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OA011-02. Defining the mechanisms of HIV entry and interactions with the female genital tract

AM Carias*[1], S McCoombe[1], M McRaven[1], M Anderson[1], R Veazey[2] and TJ Hope[1]

Address: [1]Cell and Molecular Biology, Northwestern University, Chicago, IL, USA and [2]Tulane National Primate Center, Covington, LA, USA
* Corresponding author

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Background

To date, little is known about the mechanisms of the sexual transmission of HIV and how the virus interacts with the female genital epithelium to gain access to underlying target cells. We illustrate that HIV is able to penetrate both intact columnar and squamous epithelium in explants and the living rhesus macaque. Through a series of approaches we were able to determine the mechanism of HIV entry into these tissues.

Methods

Human cervical explants and macaque genital tracts were exposed to PA-GFP HIV. Macaques were inoculated intravaginally and genital tissues were removed 4, 12, and 24 hours post-inoculation and dissected into relevant tissue specimens. Two separate macaques were inoculated *ex vivo*. Samples were snap frozen, sectioned and stained accordingly. Fluorescent BSA was added to specimens to investigate tissue permeability. Comparison of the image z-stacks before and after photoactivation reveals viral signal, accounting for background.

Results

Within 4 hours, photoactivatable virions were observed between superficial differentiated squamous epithelial cells, with penetrating virus up to depths of 50 μm in macaques. Some virions remained for at least 24 hours, illustrating viral persistence within tissue samples. Fewer virions associated with the macaque endocervix compared to human explants. In contrast, macaque explants were very similar to human explants, indicating that the intact tubular cervix filled with mucus is an efficient barrier to HIV. Penetration of squamous epithelium was influenced by presence of cellular junctions and co-localized with the penetration of fluorescent BSA.

Conclusion

Together these results indicate that HIV can penetrate to depths in both squamous and columnar epithelium where they can interact with HIV target cells. Fluorescent BSA experiments reveal that viral depth is directly proportional to epithelial permeability and in areas where cellular junctions are absent, suggesting a diffusion-based mechanism for viral entry.